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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/267,511	03/12/99	BRENNEMAN D	015280-37700

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EXAMINER	
TURNER, S	
ART UNIT	**PAPER NUMBER**
1647	11

DATE MAILED: 10/20/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/267,511	Brenneman
Examiner	**Group Art Unit**
Sharon L. Turner, Ph.D.	1647

☒ Responsive to communication(s) filed on 8-4-00

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) 1-44 is/are pending in the applicat

Of the above, claim(s) 19-44 is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-18 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims 1-44 are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 4

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. The Art Unit of U.S. Patent application SN 09/267,511 has changed. In order to expedite the correlation of papers with the application please direct all future correspondence to Technology Center 1600, Art Unit 1647.

Election/Restriction

2. Applicant's election with traverse of Group I, claims 1-18 in Paper No. 10 is acknowledged. The traversal is on the ground(s) that there is no additional burden placed on the examiner in considering the claims of Groups I-III. This is not found persuasive because contrary to applicants assertion, the searches for the methods of Groups I-II and the compositions of Group III are not coextensive. For example, the search for Group I requires a search of methods for reducing a condition associated with fetal alcohol syndrome, the search for Group II requires a search of methods for reducing neuronal cell death and further the compositions of Group III differ as claimed from the compositions of Groups I and II. Applicants further submit that the methods of Groups I and II are incorrectly classified and thus that the office has not met the initial burden of properly establishing reasons for insisting upon restriction based on different classification in the art. In response, the examiner notes that the method of Group I may be alternatively classified in class 514, subclass 16 and that the method of Group II may be alternatively classified in class 424, subclass 185.1.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 19-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-3, 12 and 14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification discloses SEQ ID NO's:1-2 and 21-26 which correspond respectively to the ADNF amino acid sequences. These SEQ ID NO's meet the written description provisions of 35 USC 112, first paragraph. However, the claims are directed to or encompass corresponding sequences from other species, mutated sequences, allelic variants, splice variants and combinations. None of these sequences meets the written description provision of 35 USC 112, first paragraph.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that, "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is for purposes of the 'written description' inquiry, whatever is now claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO's:1-2 and 21-26 of the instant application, the skilled artisan cannot envision the detailed chemical structure of the encompassed nucleic and amino acids and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The specific nucleic and amino acids are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Therefore, only SEQ ID NO's:1-2 and 21-26 , but not the full breadth of claims meet the written description provision of 35 USC 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

6. Claims 1-18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specifications disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without undue experimentation. The factors relevant to this discussion include the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims.

Claims 1-18 are drawn to a method of reducing a condition associated with fetal alcohol syndrome in a subject exposed to alcohol *in utero*. The method comprises administering ADNF polypeptides in an amount sufficient to reduce a condition associated with fetal alcohol syndrome.

The specification teaches pretreatment of animals with ADNF polypeptides NAP and SAL as specified at pp. 22-23 of the specification, **prior** to exposure with ethyl alcohol. This pretreatment produced significant differences in Fetal Demise, Fetal Weight, and Fetal brain Weight in animals subsequently exposed to alcohol as depicted in Figures 1-3. However, such protocol fails to support a reduction in a condition associated with fetal alcohol syndrome, which syndrome indicates a developed condition as claimed. In other words, the specification fails to show that the injected peptides affect a condition associated with fetal alcohol syndrome

contracted *in utero* by exposure to alcohol as claimed. The experimental animals lack affliction with fetal alcohol syndrome because the animals lack prior exposure to alcohol. Thus, the specification merely shows that administration of said peptides (as specified pp. 22-23 and Figs 1-3) affect Fetal Demise, Fetal Weight, Fetal brain Weight and VIP mRNA in animals subsequently exposed to alcohol as compared to controls, which showing is not commensurate in scope with the claimed invention. Therefore, the skilled artisan would require further undue experimentation to determine if such peptide administration is capable of reducing any condition associated with fetal alcohol syndrome as claimed.

The art teaches that fetal alcohol syndrome and alcohol-related neurodevelopmental disorders are characterized by life-long compromises in learning, memory and adaptive responses, in which to date there are no clinical remedies to recommend for either specific or global fetal alcohol effects, see in particular abstract, Hannigan et al., Neurotoxic. & Teratol., Jan-Feb 2000, 22(1):103-111. In addition, Hannigan et al., caution that the findings in rodents using basic research models to assess the potential of treatments for neurobehavioral effects of prenatal alcohol exposure, and the application of such findings to children may not be straight forward, i.e., they are unpredictable, see in particular abstract. Thus, the specification lacks the guidance required by the skilled artisan to develop and test with reasonable probability the effect of the claimed peptides for any condition associated with fetal alcohol syndrome including compromises in learning, memory and adaptive responses.

Further, with regard to applicants limitation "in an amount sufficient to reduce the condition associated with fetal alcohol syndrome", the claims fail to specify any amount in correlation to any specified condition associated with fetal alcohol syndrome. Thus, the skilled artisan would require further undue experimentation to define suitable conditions which may be affected and to determine the amount of ADNF required to produce such effect.

In addition, the skilled artisan recognizes the unpredictability in the art associated with the prediction of peptide function based upon divergent structure, see in particular Skolnick et al., Trends in Biotech 18(1):34-39, 2000, abstract and Box 2. Thus, for those divergent peptide structures, the skilled artisan would be required to perform further undue experimentation to discover those peptides which possess the properties of alleviating any condition associated with fetal alcohol syndrome.

In regard to claim 14, the skilled artisan recognizes that expression of polypeptides from nucleic acid requires the presence of promoter and expression sequences which direct expression in the host cell. Yet, claim 14 recites administration of a nucleic acid in the absence of such sequences. Further, the specification fails to teach the nucleic acid to be administered, suitable *in vivo* expression and delivery systems such that expression of the ADNF polypeptide is achieved, and delivery to the host such that a condition associated with fetal alcohol syndrome is reduced. The skilled artisan recognizes the difficulties and unpredictability associated with the development of such systems for nucleic acid/gene therapy, see in particular Smith AE., Ann. Rev. of Microbiol., 49:807-38, 1995, which teach a wide variety of problems that differ with

each potential therapeutic application for the design, production and application of viral vectors, abstract and Mahato et al., J. of Drug Targeting, 4(6):337-57, 1997 for a discussion of the challenges encountered in the development of the maintenance of concentrations and relevant vicinity of nucleic acid drug for delivery *in vivo*, see in particular abstract. Thus, the skilled artisan would be required to perform further undue experimentation to define the nucleic acid to be delivered and a suitable expression system such that *in vivo* delivery of ADNF is achieved at levels and locales effective to reduce a condition associated with fetal alcohol syndrome. Thus, for these reasons, it would take further undue experimentation on behalf of the skilled artisan to make and to use the claimed invention.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-2 are indefinite with respect to the recitations "ADNF", "ADNF I" and "ADNF III" because such recitation are neither defined or readily recognized in the art. The metes and bounds of the encompassed polypeptides are indefinite.

Claim 3(c) and 12 are indefinite with respect to the recitations "a combination" and "the ADNF polypeptide" because it is unclear whether applicants are intending to recite a single

peptide which comprises the sequences of SEQ ID NOs:3 and 4, or alternatively if the intention is to recite a composition comprising a first peptide comprising SEQ ID NO:3 and a second peptide comprising SEQ ID NO:4. The claim language should be amended to clearly indicate the combination(s) required.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-6 and 15-18 are rejected under 35 U.S.C. 102(b) as being anticipated by WO96/11948, Brenneman et al., 25 April 1996.

Brenneman et al., 1996 teach ADNF I polypeptides including sequences of SEQ ID Nos:1, 3, 21, and 22, see in particular claim 3 and Figure 7 in a method of administration see in particular claims 6-23. ADNF-9 and -14 peptides are also administered nasally at 1ug/day for alleviation of learning impairment. The peptides are inherently administered to an animal in an effective amount to reduce a condition associated with fetal alcohol syndrome including decreased body weight, decreased brain weight, decreased VIP mRNA and death, absent evidence to the contrary. Because the condition and effective amount are not specified in instant

claims and because learning impairment is a condition of fetal alcohol syndrome, see in particular Hannigan et al., as set forth above, the reference teachings anticipate the claimed invention.

11. Claims 1-3, 7-11 and 15-18 are rejected under 35 U.S.C. 102(a) as being anticipated by WO98/30452, Gozes et al., 13 August 1998.

Gozes et al., teach ADNF III polypeptides corresponding to SEQ ID Nos:2, 4, and 23-26, see in particular p. 58, lines 1-20 and SEQ ID Nos:1, 3, 10, 17 and 18. Claims 30 -50 define methods of administering the claimed polypeptides. Pages 80, line 26- p. 81, line 15 and Figures 8 and 10 illustrate amelioration of impaired learning and memory via administration of NAP (ADNF) polypeptides. The peptides are inherently administered to an animal in an effective amount to reduce a condition associated with fetal alcohol syndrome including decreased body weight, decreased brain weight, decreased VIP mRNA and death, absent evidence to the contrary. Because the condition and effective amount are not specified in instant claims and because learning impairment is a condition of fetal alcohol syndrome, see in particular Hannigan et al., as set forth above, the reference teachings anticipate the claimed invention.

Status of Claims

12. No claims are allowed.

13. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Sharon L. Turner, Ph.D.
October 17, 2000

CHRISTINE SAOUD
PATENT EXAMINER
Christine Saoud